A Concise and Enantioselective Approach to Cyclobutanones by Tandem Asymmetric Epoxidation and Enantiospecific Ring Expansion of Cyclopropylidene Alcohols. An Enantiocontrolled Synthesis of (+)- and (−)-α-Cuparenones

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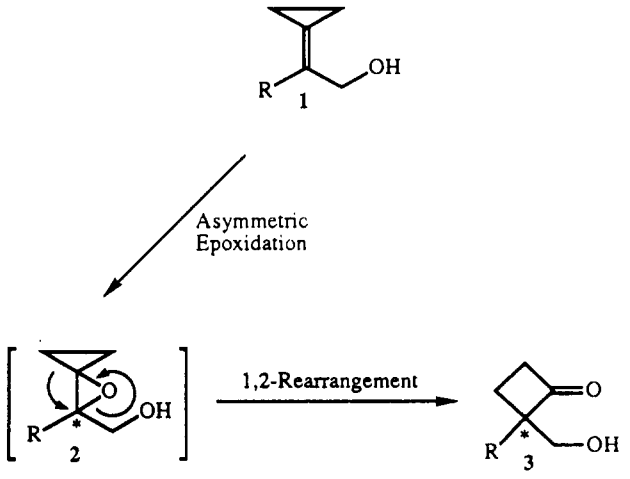
A tandem Katsuki–Sharpless asymmetric epoxidation and enantiospecific ring expansion of 2-alkyl(or 2-aryl)-2-cyclopropylideneethanols (**1a–i**) afforded chiral 1-alkyl(or 1-aryl)-1-(hydroxymethyl)cyclobutanones (**3a–i**) in high yields and high enantiomeric excess. These compounds are potentially valuable synthons for the enantioselective creation of the quaternary carbons. Hence, this enabled us to accomplish a concise and enantioselective total synthesis of both (+)- and (−)-α-cuparenones (**11**).

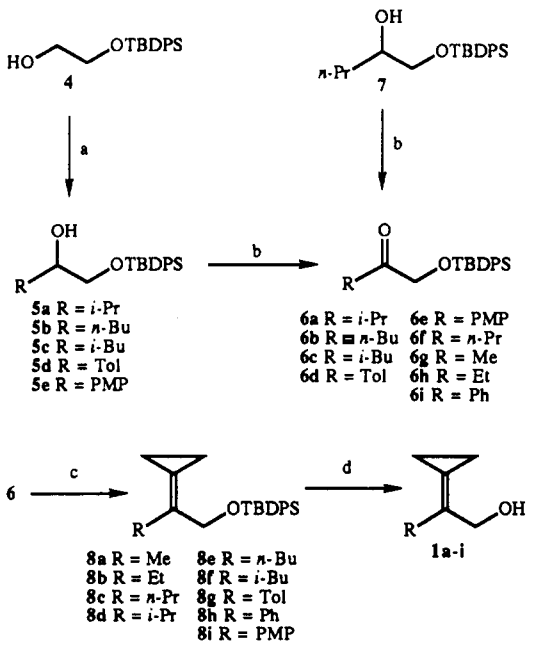
Herein, we wish to report full details for a concise and highly efficient enantioselective approach to cyclobutanones via the tandem asymmetric epoxidation and enantiospecific ring expansion of cyclopropylidene alcohols. This approach should find widespread use in organic synthesis by providing a potentially practical and generally applicable method for enantioselective creation of quaternary carbons.[1]

Cyclobutanones constitute the basic structure of many natural products[2] and are important intermediates in the synthesis of a wide range of natural products and other complex organic molecules.[3] They are most often synthesized by [2 + 2] cycloaddition reactions between ketenes and olefins,[4] and much effort has been devoted to asymmetric induction in this cycloaddition process.[5] In contrast, the studies on the asymmetric induction in the ring expansion reaction[3] of cyclopropane rings to form cyclobutane products have been limited.[6] The oxaspiropen-

Scheme I



Scheme II[a]



[a] Steps: (a) (i) DMSO, $(COCl)_2$, THF, −78 °C, 5 min then Et_3N, −78 °C; (ii) RMgBr, THF, −78 °C, 30 min; (b) PDC, CH_2Cl_2, 4 Å molecular sieves, rt, 3 h; (c) Ph_3P^+–◁ Br^-, NaH, TDA-1, THF, rt → 62 °C, 1 h; (d) n-Bu_4NF, THF, rt, 1.5 h.

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Table I. Tandem Katsuki–Sharpless Asymmetric Epoxidation and 1,2-Rearrangement of 1a–i[a]

entry	substrate R	tartrate	$Ti(O^iPr)_4$ (equiv)	TBHP (equiv)	time (h)	temp (°C)	product (%)	$[\alpha]^{23}_D$ (deg)	opt yield[b] (% ee)
1	1a; Me	(-)-DET	0.5	2	48	-40	(S)-3a (52)	-17.6	87
2	1a; Me	(-)-DET	1	3	24	-50	(S)-3a (53)	-17.9	89
3	1a; Me	(-)-DIPT	1	1.7	24	-50	(S)-3a (38)	-18.5	93
4	1a; Me	(+)-DIPT	1	1.7	24	-50	(R)-3a (54)	+18.2	92
5	1b; Et	(-)-DIPT	1	1.8	24	-50	(S)-3b (80)	+46.0	96
6	1c; *n*-Pr	(-)-DET	1	1.6	48	-50	(S)-3c (70)	+36.9	93
7	1d; *i*-Pr	(-)-DET	1	2.3	48	-50	(S)-3d (73)	+101.4	89
8	1e; *n*-Bu	(-)-DET	1	1.8	48	-50	(S)-3e (70)	+37.3	94
9	1f; *i*-Bu	(-)-DET	1	2.0	48	-50	(S)-3f (96)	+26.2	91
10	1g; Tol	(-)-DET	1	1.8	48	-50	(R)-3g (76)	+53.5	79
11	1g; Tol	(+)-DET	1	2.5	48	-50	(S)-3g (75)	-48.4	78
12	1h; Ph	(-)-DET	1	1.7	48	-50	(R)-3h (89)	+56.2	83
13	1i; PMP	(-)-DET	1	2.4	48	-50	(R)-3i (82)	+47.2	73

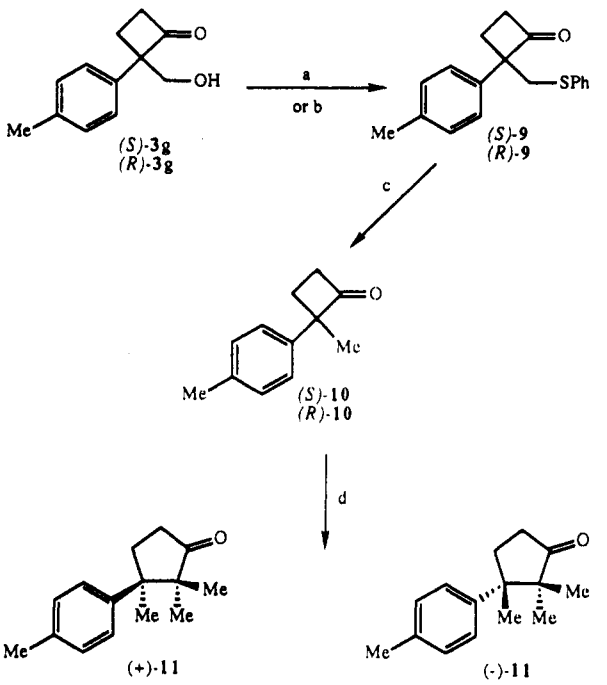
[a] Unless otherwise stated, the reaction was carried out in CH_2Cl_2 in the presence of 3-Å molecular sieves. [b] Estimated by ^1H NMR analysis (500 MHz) of [α-methoxy-α-(trifluoromethyl)phenylacetic acid (MTPA)] using corresponding racemic samples which were prepared by the epoxidation [*m*-chloroperbenzoic acid (*m*-CPBA)] accompanied by 1,2-rearrangement of 1a–i.

tanes, strained epoxides, are known to be very labile toward acid-catalyzed rearrangements accompanied by carbon-bond migration leading to cyclobutanones,[3a,7] and this process has been shown to be concerted leading to the inversion of configuration at the migration terminus. We were intrigued by the possibility that the Katsuki–Sharpless asymmetric epoxidation[8] of the cyclopropylidene alcohol **1** might give the very labile chiral hydroxyoxaspiropentanes **2** as initial products and then rearrange to chiral cyclobutanones **3** in an enantiospecific manner under the reaction conditions (Scheme I). We therefore examined the Katsuki–Sharpless asymmetric epoxidation of cyclopropylidene alcohols **1**, which led us to develop the concise and highly enantioselective method for the synthesis of chiral cyclobutanones and hence an enantiocontrolled approach to (+)- and (-)-α-cuparenones **11**.

Results and Discussion

The preparation of the substituted cyclopropylidene alcohols **1**, substrates for the Katsuki–Sharpless asymmetric epoxidation, was as follows (Scheme II). The ethylene glycol mono-*tert*-butyldiphenylsilyl (TBDPS) ether **4** was oxidized under Swern conditions [dimethyl sulfoxide (DMSO), $(COCl)_2$, CH_2Cl_2; Et_3N] to give [(*tert*-butyldiphenylsilyl)oxy]acetaldehyde which was directly subjected to Grignard reactions (RMgX, THF) to give alcohols **5a–e** in moderate to high overall yields in each case. The ketones **6a–f** were obtained by oxidation [pyridinium dichromate (PDC), CH_2Cl_2] of **5a–e** and **7**, respectively. Ketones **6g,h** were derived from the direct silylation [TBDPSCl, imidazole, dimethylaminopyridine (DMAP), DMF] of hydroxyacetone, 1-hydroxy-2-butanone, and hydroxyacetophenone, respectively. Ketones **6a–i** thus obtained were then converted into the cyclopropylidene alcohol TBDPS ethers **8a–i** in moderate to high yields in each case by Wittig reaction with cyclopropylidenetriphenylphosphorane under McMurry's conditions[9] using tris[2-(2-methoxyethoxy)ethyl]amine (TDA-1) as a catalyst. Finally, the deprotection of **8a–i** with tetra-*n*-butylammonium fluoride (TBAF) furnished quantitatively the cyclopropylidene alcohols **1a–i**, respectively.

Scheme III[a]



[a] Steps: (a) (i) MsCl, DMAP, Et_3N, rt, 3 h, CH_2Cl_2; (ii) PhSNa, DMF, rt, 20 h; (b) PhSPh, *n*-Bu_3P, THF, ref, 10 h; (c) Raney Ni (W 2), acetone, rt, 15 min; (d) ref 14.

Asymmetric epoxidation of these alcohols **1a–i** was then carried out with *tert*-butyl hydroperoxide (TBHP) in the presence of diethyl D-(-)- and L-(+)-tartrate [(-)-DET and (+)-DET] or diisopropyl D-(-)- and L-(+)-tartrate [(-)-DIPT and (+)-DIPT], titanium tetraisopropoxide [$Ti(O^iPr)_4$], and 3-Å molecular sieves[10] (Table I).

The absolute configuration and optical purity of **3a** were determined unambiguously by the direct comparison of its optical rotation with that [$[\alpha]^{22}_D$ -18.5° (*c* 0.94, $CHCl_3$)] of an authentic sample[6h] and also by ^1H NMR analysis (500 MHz) of MTPA ester. Other aliphatic substituted cyclo-

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propylidene alcohols (entries 5–9) were also obtained in high enantiomeric excess. Similarly, in aromatic substituted series (entries 10–12), this tandem reaction proceeded in a highly enantioselective manner. Hence, this tandem asymmetric epoxidation and ring expansion proceeds with complete transfer of the chirality of in situ generated epoxy alcohol **2**, and the observed stereoselectivity can be interpreted to arise from the concerted anti 1,2-migration of the C–C bond of the cyclopropane ring to the epoxide moiety.

This versatile method for the enantioselective preparation of either enantiomer of the chiral cyclobutanones led us to develop a concise synthesis of both (–)-[11] and (+)-α-cuparenones[12] [(–)-**11** and (+)-**11**] which have been shown to occur in nature in both enantiomeric forms (Scheme III). Thus, standard substitution of the hydroxy group of (*S*)-**3g** with a phenylthio group was achieved by two methods (a and b), namely via the corresponding mesylate [(i) methanesulfonyl chloride (MsCl), DMAP, triethylamine; (ii) PhSNa, DMF], and direct substitution with thiophenol by following Hata's procedure[13] in moderate (47%) and high (90%) yield, respectively, gave the sulfide (*R*)-**9**. The sulfide (*R*)-**9** thus obtained was then desulfurized by Raney Ni (W_2) in acetone to afford the methyl analogue (*S*)-**10** in high yield. By following the same procedure as described in ref 14, the cyclobutanone (*S*)-**10** was converted into (+)-α-cuparenone (**11**) [$[\alpha]^{24}_D$ +129.3° (*c* 0.98, $CHCl_3$) (lit.[12] $[\alpha]_D$ +170°, $CHCl_3$)]. This also shows a formal total synthesis of (–)-α-cuparenone (**11**) starting from (*R*)-**3g** by using the same procedure described for (+)-α-cuparenone, confirming the absolute configuration of the both hydroxymethylcyclobutanones (*S*)-**3g** and (*R*)-**3g**.

Thus, with easy access to the starting cyclopropylidene alcohol, the generally high degree of asymmetric induction, and the versatility to produce either enantiomers, the reported procedure provides an efficient means for the construction of chiral quaternary carbons useful for the synthesis of more complex optically active compounds.

Experimental Section

General Procedure. All reactions were carried out under a positive atmosphere of dry N_2 unless indicated. Solvents were freshly distilled prior to use: THF and Et_2O were distilled from sodium benzophenone; DMSO, DMF, CH_2Cl_2, and Et_3N were distilled from CaH_2 and kept over 4 Å molecular sieves. The phrase "residue upon workup" refers to the residue obtained when the organic layer was separated and dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. Silica gel column chromatography was carried out with Wako gel C-200, while Merck kieselgel 60 Art. 9385 was used for flash chromatography.

2-(*tert*-Butyldiphenylsiloxy)ethanol (4). To a stirred solution of ethylene glycol (10.7 mL, 192 mmol), Et_3N (30 mL, 215 mmol), and a catalytic amount of DMAP in CH_2Cl_2 (200 mL) was added TBDPSCl (10 mL, 38.5 mmol) at 0 °C, and stirring was continued for 10 h at rt. The reaction mixture was washed with 10% HCl, saturated aqueous $NaHCO_3$, and NaCl. The residue upon workup was chromatographed on silica gel with hexane–AcOEt (9:1 v/v) to give the monosilyl ether **4** (9.92 g, 86%) as a colorless oil: IR (neat) 3400 (OH), 1590 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.09 (9 H, s, $SiCMe_3$), 2.14 (1 H, br s, OH), 3.72 (4 H, br s, CH_2CH_2), 7.31–7.77 (10 H, m, $SiPh_2$); MS *m/z* 243 (M^+ – 57). Anal. Calcd for $C_{18}H_{24}O_2Si$: C, 71.95; H, 8.07. Found: C, 71.70; H, 8.05.

General Procedure for the Preparation of the Monosilyl Ether of Alkylated Diols from Ethylene Glycol Monosilyl Ether 4. Preparation of 1-(*tert*-Butyldiphenylsiloxy)-3-methyl-2-butanol (5a). To a stirred solution of DMSO (1.2 mL, 16.9 mmol) in THF (40 mL) was added $(COCl)_2$ (1.2 mL, 13.8 mmol) at –78 °C. After the mixture had been stirred for 5 min at –78 °C, a solution of the alcohol **4** (2.15 g, 7.16 mmol) in THF (20 mL) was added. After having been stirred for 30 min followed by addition of Et_3N (4 mL, 28.7 mmol), the mixture was stirred for 20 min at –78 °C, and stirring was continued until the reaction temperature rose to rt. The reaction mixture was cooled to –78 °C and treated with a solution of 0.7 M isopropylmagnesium bromide in THF (30 mL, 21 mmol), and stirring was continued for 30 min at the same temperature. The reaction mixture was quenched with 10% HCl solution and extracted with Et_2O. The combined extracts were washed with saturated aqueous $NaHCO_3$ and NaCl. The residue upon workup was chromatographed on silica gel with hexane–AcOEt (9:1, v/v) to give the alcohol **5a** (1.74 g, 71%) as a colorless oil: IR (neat) 3575, 3470 (OH), 1585 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.80, 0.94 (each 3 H, each d, each *J* = 7 Hz, $CHMe_2$), 1.07 (9 H, s, $SiCMe_3$), 1.26–1.86 (1 H, m, $CHMe_2$), 2.55 (1 H, d, *J* = 1.5 Hz, OH), 3.27–3.85 (3 H, m, CHOH and CH_2O), 7.32–7.72 (10 H, m, $SiPh_2$); MS *m/z* 285 (M^+ – 57). Anal. Calcd for $C_{21}H_{28}O_2Si$: C, 73.63; H, 8.83. Found: C, 73.86; H, 8.80.

1-(*tert*-Butyldiphenylsiloxy)-2-hexanol (5b): yield 90%; colorless oil; IR (neat) 3590, 3450 (OH), 1585 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.87 (3 H, t, *J* = 7 Hz, Me), 1.09 (9 H, s, $SiCMe_3$), 1.18–1.45 (6 H, m, 3 × CH_2), 2.55 (1 H, d, *J* = 2 Hz, OH), 3.47–3.81 (3 H, m, CHOH, CH_2O), 7.31–7.77 (10 H, m, $SiPh_2$); MS *m/z* 299 (M^+ – 57). Anal. Calcd for $C_{22}H_{32}O_2Si$: C, 74.10; H, 9.05. Found: C, 74.36; H, 9.12.

1-(*tert*-Butyldiphenylsiloxy)-4-methyl-2-pentanol (5c): yield 76%; colorless oil; IR (neat) 3600, 3470 (OH), 1585 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.88 (6 H, d, *J* = 6 Hz, $CHMe_2$), 1.08 (9 H, s, $SiCMe_3$), 1.10–1.90 (3 H, m, CH_2CHMe_2), 3.33–3.90 (3 H, m, CHOH, CH_2O), 7.31–7.77 (10 H, m, $SiPh_2$); MS *m/z* 299 (M^+ – 57). Anal. Calcd for $C_{22}H_{32}O_2Si$: C, 74.10; H, 9.05. Found: C, 74.12; H, 9.03.

2-(*tert*-Butyldiphenylsiloxy)-1-(*p*-tolyl)ethanol (5d): yield 98%; colorless oil; IR (neat) 3570, 3450 (OH), 1585 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.08 (9 H, s, $SiCMe_3$), 2.30 (3 H, s, Me), 2.98 (1 H, br s, OH), 3.61 (1 H, dd, *J* = 8 and 10 Hz, CH(H)O), 3.77 (1 H, dd, *J* = 4 and 8 Hz, CH(H)O), 4.27 (1 H, dd, *J* = 4 and 10 Hz, CHO), 7.01–7.71 (14 H, m, MeC_6H_4, $SiPh_2$); MS *m/z* 333 (M^+ – 57). Anal. Calcd for $C_{25}H_{30}O_2Si$: C, 76.88; H, 7.74. Found: C, 77.05; H, 8.01.

2-(*tert*-Butyldiphenylsiloxy)-1-(*p*-methoxyphenyl)-1-ethanol (5e): yield 98%; colorless prisms; mp 73–74 °C (from hexane); IR (neat) 3450 (OH), 1610, 1585 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.08 (9 H, s, $SiCMe_3$), 2.96 (1 H, d, *J* = 2 Hz, OH), 3.50–3.83 (2 H, m, CH_2O), 3.77 (3 H, s, OMe), 4.68–4.82 (1 H, m, CHOH), 6.81, 7.20 (each 2 H, each d, *J* = 9 Hz, $MeOC_6H_4$), 7.31–7.70 (10 H, m, $SiPh_2$); MS *m/z* 349 (M^+ – 57). Anal. Calcd for $C_{25}H_{30}O_3Si$: C, 73.85: H, 7.44. Found: C, 73.56; H, 7.44.

1-(*tert*-Butyldiphenylsiloxy)-2-pentanol (7). To a stirred solution of 1,2-pentanediol (2.91 g, 28 mmol), Et_3N (5 mL, 35.9 mmol), and a catalytic amount of DMAP in CH_2Cl_2 (60 mL) was added *tert*-butylchlorodiphenylsilane (3.28 g, 11.9 mmol) at 0 °C, and stirring was continued for 10 h. The reaction mixture was diluted with CH_2Cl_2 and washed with 10% HCl, saturated aqueous $NaHCO_3$, and NaCl. The residue upon workup was chromatographed on silica gel with hexane–AcOEt (96:4 v/v) to give the monosilyl ether **7** (9.48 g, 99%) as a colorless oil: IR (neat) 3580, 3450 (OH), 1585 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.89 (3 H, t, *J* = 8 Hz, Me), 1.10 (9 H, s, $SiCMe_3$), 1.23–1.50 (4 H, m, CH_2CH_2), 2.49 (1 H, br s, OH), 3.36–3.81 (2 H, s, CH_2O), 7.31–7.74 (10 H, m, $SiPh_2$); MS *m/z* 285 (M^+ – 57). Anal. Calcd for $C_{21}H_{30}O_2Si$: C, 73.64; H, 8.83. Found: C, 73.89; H, 8.83.

1-(*tert*-Butyldiphenylsiloxy)-2-propanone (6g). To a stirred solution of hydroxyacetone (1.35 mL, 19.7 mmol), imidazole (1.3 g, 19.1 mmol), and a catalytic amount of DMAP in DMF (60 mL) was added *tert*-butylchlorodiphenylsilane (4.4 mL, 16.9 mmol)

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(14) Gadwood, R. C. *J. Org. Chem.* **1983**, *48*, 2098.

at 0 °C, and stirring was continued for 10 h at rt. The reaction mixture was diluted with ether and washed with 10% HCl, saturated aqueous $NaHCO_3$, and NaCl. The residue upon workup was chromatographed on silica gel with hexane–AcOEt (97:3 v/v) to give the silyl ether **6g** (4.87 g, 100%) as a colorless oil: IR (neat) 1720 (C=O), 1585 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.21 (9 H, s, $SiCMe_3$), 2.27 (3 H, s, COMe), 4.15 (2 H, s, CH_2), 7.26–7.77 (10 H, m, $SiPh_2$); MS m/z 255 (M^+ – 57). Anal. Calcd for $C_{19}H_{24}O_2Si$: C, 73.03; H, 7.74. Found: C, 73.27; H, 7.85.

1-(*tert*-Butyldiphenylsiloxy)-2-butanone (6h). 1-Hydroxy-2-butanone (3.08 g, 34.9 mmol) was subjected to the same reaction conditions as in the case of **6g** described above to give the silyl ether **6h** (11.4 g, 100%) as a colorless oil: IR (neat) 1735, 1720 (C=O) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.04 (3 H, t, J = 7.5 Hz, Me), 1.10 (9 H, s, $SiCMe_3$), 2.66 (2 H, q, J = 7.5 Hz, CH_2Me), 4.18 (2 H, s, CH_2O), 7.30–7.72 (10 H, m, $SiPh_2$); MS m/z 269 (M^+ – 57). Anal. Calcd for $C_{20}H_{26}O_2Si$: C, 73.57; H, 8.03. Found: C, 73.50; H, 8.02.

(*tert*-Butyldiphenylsiloxy)acetophenone (6i). Hydroxyacetophenone (1.6 g, 11.8 mmol) was silylated by following exactly the same procedure described for **6g** and **6h** to give the silyl ether **6i** (4.39 g, 100%) as colorless needles: mp 80–81 °C (from hexane); IR ($CHCl_3$) 1705 (C=O), 1600, 1585 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.11 (9 H, s, $SiCMe_3$), 4.91 (2 H, s, CH_2O), 7.31–7.78 (15 H, m, Ph, $SiPh_2$); MS m/z 317 (M^+ – 57). Anal. Calcd for $C_{24}H_{26}O_2Si$: C, 76.96; H, 7.00. Found: C, 77.02; H, 7.06.

General Procedure for the Preparation of Alkylated α-Siloxy Ketones from Monosilyl Ethers of Alkylated Diols. Preparation of 1-(*tert*-Butyldiphenylsiloxy)-2-pentanone (6f). To a stirred suspension of PDC (7 g, 18.6 mmol) and 4-Å molecular sieves (3 g) in CH_2Cl_2 (20 mL) was added the alcohol **7** (4.3 g, 12.6 mmol) at rt, and stirring was continued for 3 h at the same temperature. The reaction mixture was diluted with Et_2O and filtered through Celite. The residue resulted from evaporation of the solvent was chromatographed on silica gel with hexane–AcOEt (98:2 v/v) to give the ketone **6f** (3.71 g, 87%) as an oil: IR (neat) 1730, 1720 (C=O), 1585 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.89 (3 H, t, J = 8 Hz, Me), 1.13 (9 H, s, $SiCMe_3$), 1.59 (2 H, tq, J = 7 and 8 Hz, CH_2CH_2Me), 2.48 (2 H, t, J = 7 Hz, $COCH_2$), 4.18 (2 H, s, CH_2O), 7.31–7.74 (10 H, m, $SiPh_2$); MS m/z 283 (M^+ – 57). Anal. Calcd for $C_{21}H_{28}O_2Si$: C, 74.07; H, 8.29. Found: C, 74.20; H, 8.40.

1-(*tert*-Butyldiphenylsiloxy)-3-methyl-2-butanone (6a): yield 82%; colorless oil; IR (neat) 1735, 1715 (C=O) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.03 (6 H, d, J = 7 Hz, $CHMe_2$), 1.11 (9 H, s, $SiCMe_3$), 2.13–2.69 (1 H, m, $CHMe_2$), 4.27 (2 H, s, CH_2O), 7.32–7.72 (10 H, m, $SiPh_2$); MS m/z 283 (M^+ – 57). Anal. Calcd for $C_{21}H_{28}O_2Si$: C, 74.07; H, 8.29. Found: C, 74.17; H, 8.26.

1-(*tert*-Butyldiphenylsiloxy)-2-hexanone (6b): yield 90%; colorless oil; IR (neat) 1735, 1720 (C=O), 1585 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.77–1.64 (7 H, m, CH_2CH_2Me), 1.00 (9 H, s, $SiCMe_3$), 2.49 (2 H, t, J = 7 Hz, CH_2CO), 4.17 (2 H, s, CH_2O), 7.31–7.77 (10 H, m, $SiPh_2$); MS m/z 297 (M^+ – 57). Anal. Calcd for $C_{22}H_{30}O_2Si$: C, 74.53; H, 8.53. Found: C, 74.69; H, 8.52.

1-(*tert*-Butyldiphenylsiloxy)-4-methyl-2-pentanone (6c): yield 81%; colorless oil; IR (neat) 1735, 1720 (C=O), 1585 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.87 (6 H, d, J = 7 Hz, $CHMe_2$), 1.10 (9 H, s, $SiCMe_3$), 1.96–2.38 (3 H, m, CH_2CH), 4.15 (2 H, s, CH_2O), 7.30–7.74 (10 H, m, $SiPh_2$); MS m/z 297 (M^+ – 57). Anal. Calcd for $C_{22}H_{30}O_2Si$: C, 74.53; H, 8.53. Found: C, 74.56; H, 8.58.

(*tert*-Butyldiphenylsiloxy)methyl Tolyl Ketone (6d): yield 86%; colorless needless; mp 100–101 °C (from hexane); IR ($CHCl_3$) 1705 (C=O), 1610, 1585 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.10 (9 H, s, $SiCMe_3$), 2.38 (3 H, s, Me), 4.89 (2 H, s, CH_2O), 7.13–7.80 (14 H, m, C_6H_4, $SiPh_2$); MS m/z 331 (M^+ – 57). Anal. Calcd for $C_{25}H_{28}O_2Si$: C, 77.27; H, 7.26. Found: C, 77.41; H, 7.34.

(*tert*-Butyldiphenylsiloxy)methyl *p*-Methoxyphenyl Ketone (6e): yield 91%; colorless prisms; mp 49–50 °C (from hexane); IR ($CHCl_3$) 1700 (C=O), 1600 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.12 (9 H, s, $SiCMe_3$), 3.84 (3 H, s, OMe), 4.85 (2 H, s, CH_2O), 6.88, 7.85 (each 2 H, each d, J = 9 Hz, C_6H_4), 7.31–7.80 (10 H, m, $SiPh_2$); MS m/z 347 (M^+ – 57). Anal. Calcd for $C_{25}H_{28}O_3Si$: C, 74.22; H, 6.98. Found: C, 74.18; H, 6.98.

General Procedure for the Preparation of Cyclopropylideneethyl Silyl Ethers. Preparation of 1-(*tert*-Butyldiphenylsiloxy)-2-cyclopropylidenepropane (8a). To a stirred suspension of NaH (1.4 g, of 60% oil suspension, 35 mmol) in THF (40 mL) was added cyclopropyltriphenylphosphonium bromide (13.5 g, 35.23 mmol) at rt. After the mixture had been stirred for 10 h at 62 °C, a solution of the ketone **6a** (5.5 g, 17.6 mmol) and TDA-1 (0.56 mL, 1.75 mmol) in THF (20 mL) was added in 30 min, and stirring was continued for 1 h at the same temperature. The reaction mixture was diluted with water and extracted with Et_2O. The combined extracts were washed with saturated aqueous NaCl. The residue upon workup was chromatographed on silica gel with hexane–EtOAc (99:1 v/v) to give the cyclopropylideneethyl silyl ether **8a** (5.9 g, 100%) as a colorless oil: IR (neat) 1585 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.89 (4 H, br s, cyclopropylidene), 1.05 (9 H, s, $SiCMe_3$), 1.90 (3 H, t, J = 1.5 Hz, Me), 4.29 (2 H, s, CH_2O), 7.21–7.77 (10 H, m, $SiPh_2$); MS m/z 336 (M^+). Anal. Calcd for $C_{22}H_{28}OSi$: C, 78.52; H, 8.39. Found: C, 78.33; H, 8.42.

1-(*tert*-Butyldiphenylsiloxy)-2-cyclopropylidenebutane (8b): yield 69%; colorless oil; IR (neat) 1590 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.69–1.09 (4 H, m, cyclopropylidene), 1.04 (9 H, s, $SiCMe_3$), 1.10 (3 H, t, J = 9 Hz, Me), 2.33 (2 H, q, J = 9 Hz, CH_2Me), 4.30 (2 H, s, CH_2O), 7.30–7.75 (10 H, m, $SiPh_2$); MS m/z 293 (M^+ – 57). Anal. Calcd for $C_{23}H_{30}OSi$: C, 78.80; H, 8.63. Found: C, 79.18; H, 8.84.

1-(*tert*-Butyldiphenylsiloxy)-2-cyclopropylidenepentane (8c): yield 81%; colorless oil; IR (neat) 1585 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.76–1.03 (4 H, m, cyclopropylidene), 0.87 (3 H, t, J = 7.5 Hz, Me), 1.05 (9 H, s, $SiCMe_3$), 1.54 (2 H, tq, J = 7.5 and 8 Hz, CH_2Me), 2.29 (2 H, t, J = 8 Hz, CH_2CH_2C=), 4.29 (2 H, s, CH_2O), 7.29–7.74 (10 H, m, $SiPh_2$); MS m/z 364 (M^+); exact mass calcd for $C_{24}H_{32}OSi$ 364.2221 (M^+), found 364.2241.

1-(*tert*-Butyldiphenylsiloxy)-2-cyclopropylidene-3-methylbutane (8d): yield 76%; colorless oil; IR (neat) 1585 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.61–1.25 (4 H, m, cyclopropylidene), 1.04 (9 H, s, $SiCMe_3$), 1.14 (6 H, d, J = 7 Hz, $CHMe_2$), 1.96–2.45 (1 H, m, $CHMe_2$), 4.31 (2 H, s, CH_2O), 7.29–7.80 (10 H, m, $SiPh_2$); MS m/z 307 (M^+ – 57); exact mass calcd for $C_{20}H_{23}OSi$ 307.1517 (M^+), found 307.1548.

1-(*tert*-Butyldiphenylsiloxy)-2-cyclopropylidenehexane (8e): yield 74%; colorless oil; IR (neat) 1585 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.70–1.75 (11 H, m, CH_2CH_2Me, cyclopropylidene), 1.07 (9 H, s, $SiCMe_3$), 2.80 (2 H, t, J = 8 Hz, CH_2C=), 4.30 (2 H, s, CH_2O), 7.30–7.78 (10 H, m, $SiPh_2$); MS m/z 378 (M^+); exact mass calcd for $C_{25}H_{34}OSi$ 378.2377 (M^+), found 378.2383.

1-(*tert*-Butyldiphenylsiloxy)-2-cyclopropylidene-4-methylpentane (8f): yield 71%; colorless oil; IR (neat) 1585 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.86 (6 H, d, J = 6 Hz, $CHMe_2$), 0.91 (4 H, m, cyclopropylidene), 1.04 (9 H, s, $SiCMe_3$), 1.75–2.21 (3 H, m, CH_2CH), 4.28 (2 H, br s, CH_2O), 7.29–7.77 (10 H, m, $SiPh_2$); MS m/z 321 (M^+ – 57). Anal. Calcd for $C_{25}H_{34}OSi$: C, 79.31; H, 9.05. Found: C, 79.16; H, 8.98.

1-(*tert*-Butyldiphenylsiloxy)-2-cyclopropylidene-2-(*p*-methoxyphenyl)ethane (8i): yield 78%; colorless prisms; mp 78–79 °C (from pentane); IR ($CHCl_3$) 1600, 1585 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.71–1.38 (4 H, m, cyclopropylidene), 1.01 (9 H, s, $SiCMe_3$), 3.83 (3 H, s, OMe), 4.72 (2 H, s, CH_2O), 6.83–7.80 (14 H, m, C_6H_4, $SiPh_2$); MS m/z 428 (M^+). Anal. Calcd for $C_{28}H_{32}O_2Si$: C, 78.46; H, 7.52. Found: C, 78.25; H, 7.63.

General Procedure for the Preparation of Cyclopropylidene Alcohols. Preparation of 2-Cyclopropylidene-2-propanol (1a). To a stirred solution of the silyl ether **8a** (760 mg, 2.26 mmol) in THF (3 mL) was added 1 M solution of $^nBu_4NF$ in THF (3.5 mL, 3.5 mmol) at rt, and stirring was continued for 1.5 h at the same temperature. The reaction mixture was diluted with water and extracted with CH_2Cl_2. The combined extracts were washed with saturated aqueous NaCl. The residue upon workup was chromatographed on silica gel with hexane–AcOEt (7:3 v/v) to give the alcohol **1a** (219 mg, 99%) as a colorless oil: IR ($CHCl_3$) 3360 (OH) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.90–1.24 (4 H, m, cyclopropylidene), 1.78 (1 H, s, OH), 1.85 (3 H, t, J = 1.5 Hz, Me), 4.21 (2 H, s, CH_2O); MS m/z 98 (M^+); exact mass calcd for $C_6H_{10}O$ 98.0731 (M^+), found 98.0754.

2-Cyclopropylidene-1-butanol (1b): yield 99%; colorless oil; IR ($CHCl_3$) 3610, 3450 (OH) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.98–1.13 (4 H, m, cyclopropylidene), 1.10 (3 H, t, J = 9 Hz, Me), 2.26 (2 H, q, J = 9 Hz, CH_2Me), 4.23 (2 H, s, CH_2O); MS m/z

95 (M^+ - 17); exact mass calcd for C_7H_{11} 95.0860 (M^+ - 17), found 95.0873.

2-Cyclopropylidene-1-pentanol (1c): yield 99%; colorless oil; IR ($CHCl_3$) 3610, 3450 (OH) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.90 (3 H, t, J = 7.5 Hz, Me), 1.05 (4 H, m, cyclopropylidene), 1.56 (2 H, tq, J = 7.5 and 8 Hz, CH_2Me), 1.79 (1 H, br s, OH), 2.22 (2 H, t, J = 8 Hz, $=CCH_2$), 4.20 (2 H, s, CH_2O); MS m/z 109 (M^+ - 17); exact mass calcd for C_8H_{13} 109.1017 (M^+ - 17), found 109.1015.

2-Cyclopropylidene-3-methyl-1-butanol (1d): yield 92%; colorless oil; IR ($CHCl_3$) 3610, 3450 (OH), 1600 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.80–1.45 (4 H, m, cyclopropylidene), 1.13 (6 H, d, J = 7 Hz, $CHMe_2$), 1.68 (1 H, br s, OH), 2.32–2.72 (1 H, m, $CHMe_2$), 4.25 (2 H, s, CH_2O); MS m/z 111 (M^+ - 15); exact mass calcd for $C_7H_{11}O$ 111.0809 (M^+ - 15), found 111.0808.

2-Cyclopropylidene-1-hexanol (1e): yield 83%: colorless oil; IR ($CHCl_3$) 3350 (OH) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.74–1.70 (11 H, m, CH_2CH_2Me, cyclopropylidene), 1.90 (1 H, s, OH), 2.23 (2 H, t, J = 8 Hz, $CH_2C=$), 4.21 (2 H, s, CH_2O); MS m/z 140 (M^+); exact mass calcd for $C_9H_{16}O$ 140.1200 (M^+), found 140.1177.

2-Cyclopropylidene-4-methyl-1-pentanol (1f): yield 98%; colorless oil; IR ($CHCl_3$) 3350 (OH) cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 0.88 (6 H, d, J = 6 Hz, $CHMe_2$), 1.07 (4 H, m, cyclopropylidene), 1.55–2.25 (3 H, m, CH_2CH), 4.21 (2 H, s, CH_2O); MS m/z 125 (M^+ - 15); exact mass calcd for $C_8H_{13}O$ 125.0966 (M^+), found 125.0939.

2-Cyclopropylidene-2-(*p*-tolyl)-1-ethanol (1g): yield 82% from **6g**; colorless needless; mp 76–77 °C (from hexane–Et_2O); IR ($CHCl_3$) 3600 (OH), 1600 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.00–1.65 (4 H, m, cyclopropylidene), 2.35 (3 H, s, Me), 4.69 (2 H, s, CH_2O), 7.18–7.58 (each 2 H, each d, J = 8 Hz, C_6H_4); MS m/z 174 (M^+); exact mass calcd for $C_{12}H_{14}O$ 174.1044 (M^+), found 174.1034.

2-Cyclopropylidene-2-phenyl-1-ethanol (1h): yield 52% from **6h**; colorless needless; mp 55–56 °C (from hexane–Et_2O); IR ($CHCl_3$) 3610, 3450 (OH), 1600 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.13–1.51 (4 H, m, cyclopropylidene), 1.56 (1 H, s, OH), 4.72 (2 H, s, CH_2O), 7.31–7.75 (5 H, m, Ph); MS m/z 160 (M^+); exact mass calcd for $C_{11}H_{12}O$ 160.0888 (M^+), found 160.0870.

2-Cyclopropylidene-2-(*p*-methoxyphenyl)ethanol (1i): yield 100%; colorless needless; mp 68–69 °C (from hexane–Et_2O); IR ($CHCl_3$) 3400 (OH), 1600 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.04–1.61 (4 H, m, cyclopropylidene), 1.90 (1 H, s, OH), 3.81 (3 H, s, OMe), 4.68 (2 H, s, CH_2O), 6.89, 7.63 (each 2 H, each d, J = 9 Hz, C_6H_4); MS m/z 190 (M^+). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.50; H, 7.52.

General Procedure for Tandem Katsuki–Sharpless Asymmetric Epoxidation and 1,2-Rearrangement of Cyclopropylidene Alcohols. Preparation of (*R*)-(+)-2-(Hydroxymethyl)-2-methylcyclobutanone (3a). To a stirred solution of the cyclopropylidene alcohol **1a** (1.13 g, 11.5 mmol) and L-(+)-DIPT (3.3 g, 14.1 mmol) in CH_2Cl_2 (20 mL) was added 3-Å molecular sieves (500 mg) at -20 °C. After having been stirred for 30 min at -20 °C, $Ti(O^iPr)_4$ (3.4 mL, 11.5 mmol) was added, and stirring was continued for 30 min at the same temperature. To this reaction mixture was added a 3.5 M solution of ^tBuOOH in CH_2Cl_2 (5.6 mL, 19.6 mmol) at -78 °C, and stirring was continued for further 24 h at -50 °C. The reaction mixture was treated with a solution of citric acid monohydrate (2.46 g, 11.7 mmol) in Et_2O–acetone (9:1 v/v) (70 mL), stirred for 1 h, and filtered through Celite. The residue upon evaporation of the solvent was chromatographed on silica gel with hexane–Et_2O (7:3 v/v) to give the cyclobutanone **3a** (711 mg, 54%) as a colorless oil: $[\alpha]^{23}_D$ +18.2° (*c* 1.0, $CHCl_3$); IR (neat) 3420 (OH), 1778 (C=O) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.22 (3 H, s, Me), 1.59–2.39 (2 H, m, CH_2), 1.90 (1 H, br s, OH), 2.80–3.24 (2 H, m, $COCH_2$), 3.52, 3.73 (each 1 H, each d, J = 9 Hz, CH_2OH); MS m/z 114 (M^+); exact mass calcd for $C_6H_{10}O_2$ 114.0680 (M^+), found 114.0681.

(*S*)-(-)-2-(Hydroxymethyl)-2-methylcyclobutanone ((*S*)-3a): yield 38%; colorless oil; $[\alpha]^{23}_D$ -18.5° (*c* 0.95, $CHCl_3$); MS m/z 114 (M^+); exact mass calcd for $C_6H_{10}O_2$ 114.0680 (M^+), found 114.0676.

(*S*)-(+)-2-Ethyl-2-(hydroxymethyl)cyclobutanone (3b): yield 80%; colorless oil; $[\alpha]^{23}_D$ +46.0° (*c* 2.2, $CHCl_3$); IR (neat) 3450 (OH), 1770 (C=O) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.94 (3 H, t, J = 8 Hz, Me), 1.51–2.20 (4 H, m, 2 × CH_2), 2.25 (1 H, br s, OH), 2.85–3.06 (2 H, m, $COCH_2$), 3.60, 3.80 (each 1 H, each d, J = 11 Hz, CH_2OH); MS m/z 128 (M^+); exact mass calcd for $C_7H_{12}O_2$ 128.0837 (M^+), found 128.0854.

(*S*)-(+)-2-Propyl-2-(hydroxymethyl)cyclobutanone (3c): yield 70%; colorless oil; $[\alpha]^{23}_D$ +36.9° (*c* 2.15, $CHCl_3$); IR (neat) 3450 (OH), 1775 (C=O) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.90 (3 H, t, J = 7.5 Hz, Me), 1.10–2.27 (6 H, m, 3 × CH_2), 2.85–3.04 (2 H, m, $COCH_2$), 3.58, 3.77 (each 1 H, each d, J = 11 Hz, CH_2OH); MS m/z 142 (M^+). Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.43; H, 10.11.

(*S*)-(+)-2-(Hydroxymethyl)-2-isopropylcyclobutanone (3d): yield 71%; colorless oil; $[\alpha]^{23}_D$ +101.4° (*c* 2.05, $CHCl_3$); IR (neat) 3500 (OH), 1780 (C=O) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.90, 0.95 (each 3 H, each d, J = 6.5 Hz, $CHMe_2$), 1.83–2.20 (3 H, m, OH, CH_2), 2.80–3.00 (2 H, m, $COCH_2$), 3.65, 3.85 (each 1 H, each d, J = 10 Hz, CH_2OH); MS m/z 142 (M^+); exact mass calcd for $C_8H_{14}O_2$ 142.0993 (M^+), found 142.0985.

(*S*)-(+)-2-Butyl-2-(hydroxymethyl)cyclobutanone (3e): yield 70%; colorless oil; $[\alpha]^{23}_D$ +37.3° (*c* 1.55, $CHCl_3$); IR (neat) 3470 (OH), 1775 (C=O) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.91 (3 H, t, J = 8 Hz, Me), 1.05–2.25 (8 H, m, $CH_2CH_2CH_2$, $COCH_2CH_2$), 2.86–3.05 (2 H, m, $COCH_2$), 3.57, 3.79 (each 1 H, each d, J = 11 Hz, CH_2O); MS m/z 139 (M^+ - 17); exact mass calcd for $C_9H_{15}O$ 139.1122 (M^+ - 17), found 139.1109.

(*R*)-(+)-2-(Hydroxymethyl)-2-isobutylcyclobutanone (3f): yield 96%; colorless oil; $[\alpha]^{23}_D$ +26.2° (*c* 2.65, $CHCl_3$); IR (neat) 3450 (OH), 1770 (C=O) cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 0.90, 0.93 (each 3 H, each d, J = 6 Hz, $CHMe_2$), 1.44–2.20 (5 H, m, CH_2CH, $COCH_2CH_2$), 2.85–3.14 (2 H, m, $COCH_2$), 3.59, 3.80 (each 1 H, each d, J = 11 Hz, CH_2O); MS m/z 156 (M^+). Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 68.99; H, 10.32.

(*R*)-(+)-2-(Hydroxymethyl)-2-(*p*-tolyl)cyclobutanone ((*R*)-3g): yield 76%; colorless oil; $[\alpha]^{23}_D$ +53.5° (*c* 2.4, $CHCl_3$); IR (neat) 3420 (OH), 1770 (C=O) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 2.32 (3 H, s, Me), 2.22–3.25 (5 H, m, OH, $COCH_2CH_2$), 3.64, 3.87 (each 1 H, each d, J = 11 Hz, CH_2O), 7.13, 7.27 (each 2 H, each d, J = 10 Hz, C_6H_4); MS m/z 190 (M^+). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.66; H, 7.48.

(*S*)-(-)-2-(Hydroxymethyl)-2-(*p*-tolyl)cyclobutanone ((*S*)-3g): yield 75%; colorless oil; $[\alpha]^{23}_D$ -48.4° (*c* 1.4, $CHCl_3$); MS m/z 190 (M^+); exact mass calcd for $C_{12}H_{14}O_2$ 190.0993 (M^+), found 190.1018.

(*R*)-(+)-2-(Hydroxymethyl)-2-phenylcyclobutanone (3h): yield 89%; colorless oil; $[\alpha]^{23}_D$ +56.2° (*c* 2.15, $CHCl_3$); IR (neat) 3450 (OH), 1780 (C=O), 1600 (C=C) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 2.09 (1 H, br s, OH), 2.23–3.17 (4 H, m, $COCH_2CH_2$), 3.69, 3.91 (each 1 H, each d, J = 11 Hz, CH_2O); MS m/z 176 (M^+). Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 74.49; H, 7.00.

(*R*)-(+)-2-(Hydroxymethyl)-2-(*p*-methoxyphenyl)cyclobutanone (3i): yield 82%; colorless oil; $[\alpha]^{23}_D$ +47.2° (*c* 2.35, $CHCl_3$); IR (neat) 3450 (OH), 1770 (C=O), cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.95 (1 H, s, OH), 2.19–3.17 (4 H, m, $COCH_2CH_2$), 3.64, 3.89 (each 1 H, each d, J = 11 Hz, CH_2O), 3.79 (3 H, s, OMe), 6.88, 7.30 (each 2 H, each d, J = 9 Hz, C_6H_4); MS m/z 206 (M^+); exact mass calcd for $C_{12}H_{14}O_3$ 206.0942 (M^+), found 206.0946.

General Procedure for the Preparation of (±)-(Hydroxymethyl)cyclobutanones. Preparation of 2-(Hydroxymethyl)-2-propylcyclobutanone (3c). To a stirred solution of the cyclopropylidene alcohol **1c** (110 mg, 0.872 mmol) in CH_2Cl_2 (5 mL) was added *m*-CPBA (80% active, 210 mg, 0.974 mmol) at 0 °C, and stirring was continued for 15 min at rt. The reaction mixture was diluted with CH_2Cl_2 and washed with 10% NaOH and saturated aqueous NaCl. The residue upon workup was chromatographed on silica gel with hexane–Et_2O (3:1 v/v) to give the (±)-cyclobutanone **3c** (112.3 mg, 91%) as a colorless oil. Other (±)-cyclobutanones were also prepared by following the same procedure described above, and all the spectral data were identical with those of the corresponding chiral samples.

General Preparation and Analysis of Mosher's Esters. The reaction was generally run on a 0.1 mmol scale under the modified procedure of Mosher's original procedure.[15] To a stirred

(15) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

solution of DMAP (0.1 mmol, 1.0 equiv), Et_3N (0.1 mL), and (*S*)-(−)-MTPA (28 mg, 0.12 mmol) in CH_2Cl_2 (1 mL) was added a solution of trifluoromethanesulfonyl chloride (TfCl) (20 mg, 0.12 mmol) at 0 °C. Immediately, a solution of the cyclobutanone (0.1 mmol) in CH_2Cl_2 (0.5 mL) was added. After ensuring complete reaction by monitoring the reaction by TLC, the reaction mixture was diluted with CH_2Cl_2 and washed with 10% HCl, saturated aqueous $NaHCO_3$, and NaCl. The residue upon workup was passed through a short plug of silica gel with hexane–AcOEt (93:7 v/v). ^1H NMR analysis in $CDCl_3$ at 500 MHz focused on CH_2OMTPA. These protons were typically observed at a diastereomeric pair of AB doublets at δ 4.15–4.70. The downfield pair at δ 4.30–4.70 was compared by integration to determine the enantiomeric excess.

(*S*)-(−)-2-[(Phenylthio)methyl]-2-(*p*-tolyl)cyclobutanone (9). (a) To a stirred solution of the (*R*)-(+)-(hydroxymethyl)-cyclobutanone **3g** (75.7 mg, 0.398 mmol), Et_3N (0.17 mL, 1.22 mmol), and a catalytic amount of DMAP in CH_2Cl_2 (2 mL) was added MsCl (0.06 mL, 0.775 mmol) at 0 °C. After being stirred for 3 h at the same temperature, the reaction mixture was diluted with CH_2Cl_2 and washed with 10% HCl, saturated aqueous $NaHCO_3$, and NaCl. The solution of the residue upon workup in DMF (2 mL) was added under stirring to the solution of sodium thiophenoxide [prepared from thiophenol (0.09 mL, 0.876 mmol) and NaH (19.2 mg of 60% oil suspension, 0.8 mmol)] in DMF (2 mL) at 0 °C, and stirring was continued for 20 h at rt. The reaction mixture was diluted with Et_2O and washed with aqueous 10% NaOH and saturated aqueous NaCl. The residue upon workup was chromatographed on silica gel with hexane–Et_2O (97:3 v/v) to give the sulfide (*S*)-(−)-**9** (51.8 mg, 46%) as a colorless oil: $[\alpha]^{23}_D$ −17.5° (*c* 1.0, $CHCl_3$); IR (neat) 1775 (C=O) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 2.33 (3 H, s, Me), 2.35–3.20 (4 H, m, $COCH_2CH_2$), 3.35 (2 H, s, CH_2S), 7.10–7.85 (9 H, m, SC_6H_5, MeC_6H_4); MS *m/z* 282 (M^+). Anal. Calcd for $C_{18}H_{18}OS$: C, 76.56; H, 6.42; S, 11.35. Found: C, 76.60; H, 6.45; S, 11.32.

By following the same procedure describe above, the (*S*)-(−)-(hydroxymethyl)cyclobutanone **3g** (210 mg, 1.11 mmol) afforded the sulfide (*R*)-(+)-**9** (145 mg, 47%) as a colorless oil: $[\alpha]^{23}_D$ +16.84° (*c* 2.9, $CHCl_3$); MS *m/z* 282 (M^+); exact mass calcd for $C_{18}H_{18}OS$ 282.1077 (M^+), found 282.1098.

(b) After a solution of the (*R*)-(+)-(hydroxymethyl)cyclobutanone **3g** (500 mg, 2.63 mmol), diphenyl disulfide (1.72 g, 7.89 mmol), and tri-*n*-butylphosphine (2.62 mL, 10.5 mmol) in THF (15 mL) had been refluxed for 10 h under stirring, the reaction mixture was diluted with ether and washed with aqueous 10% NaOH and saturated aqueous NaCl. The residue upon workup was chromatographed on silica gel with hexane–benzene (4:1 v/v) to give the sulfide (*S*)-(−)-**9** (671.5 mg, 90%) as a colorless oil which was identical in all aspects with that obtained by the method a as above.

(*R*)-(+)-2-Methyl-2-(*p*-tolyl)cyclobutanone (10). To a stirred solution of the sulfide (*S*)-(−)-**9** (50.1 mg, 0.178 mmol) in acetone (4 mL) was added Raney Ni (1.5 g) at rt. After being stirred for 15 min at rt, the reaction mixture was filtered through Celite. The residue upon evaporation of the solvent was chromatographed on silica gel with hexane–Et_2O (97:3 v/v) to give the cyclobutanone (*R*)-(+)-**10** (22.2 mg, 72%) as a colorless oil: $[\alpha]^{23}_D$ +45.7° (*c* 0.8, $CHCl_3$); IR (neat) 1780 (C=O) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.53 (3 H, s, Me), 1.97–3.20 (4 H, m, $COCH_2CH_2$), 2.34 (3 H, s, MeC_6H_4), 7.12, 7.27 (each 2 H, each d, *J* = 9 Hz, MeC_6H_4); MS *m/z* 174 (M^+); exact mass calcd for $C_{12}H_{14}O$ 174.1044 (M^+), found 174.1055.

By following the exact same procedure described above, the sulfide (*R*)-(+)-**9** (131 mg, 0.465 mmol) afforded the cyclobutanone (*S*)-(−)-**10** (68.3 mg, 72%) as a colorless oil: $[\alpha]^{23}_D$ −52.6° (*c* 2.0, $CHCl_3$); MS *m/z* 174 (M^+); exact mass calcd for $C_{12}H_{14}O$ 174.1044 (M^+), found 174.1061.

(+)-α-Cuparenone (11). A solution of isopropyl phenyl selenide (56 mg, 0.28 mmol) in THF (1 mL) was cooled to −20 °C, and a solution of *m*-CPBA (80% active, 58 mg, 0.269 mmol) in THF (1 mL) was added. After 15 min at −20 °C, the solution was cooled to −78 °C, and a solution of lithium diisopropylamide (1 M in THF, 0.68 mL, 0.68 mmol) was added. After 10 min at −78 °C, a solution of (*R*)-(+)-cyclobutanone (**10**) (42.5 mg, 0.244 mmol) in THF (1 mL) was added. After an additional 10 min at −78 °C, the reaction temperature was raised to 0 °C and stirring was continued for 5 min at the same temperature. After the reaction mixture had refluxed for 45 min, it was cooled to rt and quenched with saturated aqueous NH_4Cl. The reaction mixture was extracted with ether. The extract was washed with saturated aqueous NaCl. The residue upon workup was chromatographed on silica gel with hexane–AcEt (100:1.5) to give (+)-α-cuparenone (**11**) (14.2 mg, 27%) as a colorless oil: $[\alpha]^{24}_D$ +129.3° (*c* 0.98, $CHCl_3$); IR (neat) 1740 (C=O) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.62 (3 H, s, Me), 1.17 (3 H, s, Me), 1.25 (3 H, s, Me), 1.77–2.03 (1 H, m, CH_2CH), 2.34 (3 H, s, Me), 2.40–2.85 (3 H, m, CH_2CH), 7.15, 7.30 (each 2 H, each d, *J* = 9 Hz, MeC_6H_4); MS *m/z* 216 (M^+); exact mass calcd for $C_{15}H_{20}O$ 216.1514 (M^+), found 216.1514.

Supplementary Material Available: ^1H NMR spectra of **1a–f,h** and **8c–e** (10 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.